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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,851	05/29/2007	**William Brown**	101260-1P US	1341

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EXAMINER	
LEESER, ERICH A	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
02/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,851	BROWN ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6-27-06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *11-14* is/are allowed.

6)☒ Claim(s) *1-5,8,10 and 15* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-18-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 and 8-15 are pending and under examination.

Information Disclosure Statement

The references disclosed in the IDS dated October 18, 2006 are made of record.

Priority

Acknowledgement is made that this application is a 371 of PCT/SE05/00014, filed on January 5, 2005 and which claims foreign priority to SWEDEN 0400027-9, filed on January 9, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because while enabling for the treatment of pain, the specification does not enable the instant compounds to treat anxiety or functional gastrointestinal disorders or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

The instant invention is drawn to various diarylmethyl piperazine derivatives, compositions, preparations and methods of treating pain, anxiety and functional gastrointestinal disorders to a patient in need thereof.

The state of the prior art:

The state of the prior art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. For example, "The role of the opioid system in controlling pain, reward and addiction is well established, but its role in regulating other emotional responses is poorly documented in pharmacology." (Emphasis added). Filliol D, et al., *Mice deficient for delta- and mu-opioid receptors exhibit opposing alterations of emotional responses*, Nature genetics, (2000 Jun) Vol.

25, No. 2, pp. 195-200. This reference from the time the invention was made shows the speculative nature of treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor.

The predictability in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize, with regards to therapeutic effects, whether or not the compounds of the invention would be useful for treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor.

Amount of guidance/working examples:

Applicants provide various *in vivo* testing protocols in the specification. There are no examples in the specification; however, showing that the instant compounds can be effectively used for treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor.

The breadth of the claims:

The breadth of claims is drawn to treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor.

The quantity of undue experimentation needed:

Since the guidance and teaching provided by the specification is insufficient for treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor, one skilled in the art, even with a high level of skill, is unable to practice the invention as claimed without undue experimentation.

The level of the skill in the art:

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art; however, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases or diseases would benefit from this activity.

Taking all of the above factors into consideration, it is not seen how one of ordinary skill in the art would be able to make and use the compounds of the present invention for treating anxiety and functional gastrointestinal disorders to a patient in need thereof at the delta opioid receptor without undue experimentation.

Claim Rejections 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brown, et al., U.S. Patent No. 7,253,173. The reference teaches 4(phenyl-piperazinyl-methyl)benzamide derivatives structurally similar to instant compounds (see col. 5, compounds of formula I and definitions of R1…). The claims differ by requiring a methyl group at R1 over hydrogen of the reference. That is, the instant compounds are tertiary amines over the secondary amines of the prior art. Tertiary versus secondary amines are homologues. Mono-substituted piperazines were found unpatentable over disubstituted piperazines in *Ex Parte Weston and Hamlin*, 121 USPQ 428. The court stated "... any chemist is readily aware of the difference between secondary and tertiary amines, including their reactivities, particularly with respect to the possibility of further substitution for the H in the secondary amine." *Ex parte Bluestone*, 135 USPQ 199 and *In re Doebel*, 179 USPQ 158 further affirm that N-CH_3 is obvious over N-H. See *In re Hoeksema*, 154 USPQ 169, where the court states that secondary and primary amines are homologues and further states "...a chemist looking at the formula for another compound which differs so slightly that it is called a homolog generally expects the second compound to have properties similar to the first one." One skilled in the art would be motivated to change the compounds of the reference to arrive at the compounds of the instant application in hopes of

achieving compositions more effective in treating pain, anxiety and functional gastrointestinal disorders.

Claim Objections

Claim 9 is objected to as being dependent upon rejected independent claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

Allowable subject matter

Claims 11-14 are allowable. The closest prior art is Brown, et al., U.S. Patent No. 7,253,173. The reference discloses processes of making 4(phenyl-piperazinyl-methyl)benzamide derivatives very similar to the process claims of the instant application. The difference between the process claims of the reference and the instant process claims of the application is based on the definition of the reactants: in the reference the reactants are either alkylcarbamate or heteroaryl-CHO, whereas the instant claims require the reactants to be either halogen or non-heteroaryl-CHO.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Erich A. Leeser/

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